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APPEAL BRIEF

Attorney Docket No. 2356.0014-09

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APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:)

Luc MONTAGNIER et al.)

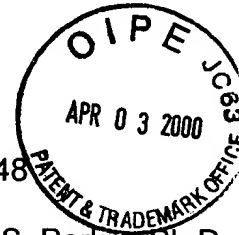
Serial No. 08/470,489)

Filed: June 6, 1995)

For: RETROVIRUS CAPABLE OF)
CAUSING AIDS, MEANS AND)
METHOD FOR DETECTING IT)
IN VITRO)

Group Art Unit: 1648

Examiner: Jeffrey S. Parkin, Ph.D.



Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

APPELLANT'S BRIEF ON APPEAL UNDER 37 C.F.R. § 1.192

This is an appeal to the Board of Patent Appeals and Interferences from the final rejection of claims 90-109 in the above-referenced patent application. The appealed claims are set forth in the attached Appendix.

Three copies of this Appeal Brief are being filed along with the required brief filing fee of \$300.00. The period for response has been extended by the filing of a petition for a four-month extension of time and the appropriate fee. The date to file this Appeal Brief ran from the October 6, 1999, Notice of Appeal. Please charge any additional fees that may be due to Deposit Account No. 06-0916.

I. Real Party in Interest

Institut Pasteur, the Assignee of this application, is the real party in interest. The assignment was recorded on November 11, 1987, at Reel 4940, starting at Frame 0135.

II. Related Appeals and Interferences

Neither Appellant, the Appellant's legal representative, or assignee are aware of any other appeals or interferences which will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. Status of Claims

The Examiner has rejected all pending claims 90-109, and Appellant filed the current Notice of Appeal on October 6, 1999, appealing the final rejection of claims 90-109.

IV. Status of Amendments

Applicant requested that the Office amend the claims on August 3, 1999. The Examiner, in the August 23, 1999, Advisory Action, refused to enter the amendments, stating that the proposed amendments change the scope of the invention and would require further consideration and/or search.

V. Summary of Invention

This invention is directed to a method of detecting HIV-2 retrovirus nucleic acid in a biological sample. The method uses hybridization techniques to detect the HIV-2

retrovirus nucleic acid. Specifically, an HIV-2 specific probe is combined with the sample under one of the following hybridization conditions:

- 42°C below the melting temperature of the probe;
- 20°C below the melting temperature of the probe; and
- 3°C below the melting temperature of the probe.

The probe is an HIV-2 nucleic acid molecule that hybridizes to HIV-2ROD genomic DNA under the same hybridization conditions. After the probe and the sample are combined under the hybridization conditions, the resulting hybrid is washed under one of the three same conditions. The hybrid is then detected.

Another embodiment of the invention further defines the HIV-2 nucleic acid probe. It can be obtained from nucleotides 1-380 of the U3/R region of HIV-2, nucleotides 1-1566 of the *gag* gene of HIV-2, nucleotides 1114-1524 of the *gag* gene, nucleotides 1-405 of the *gag* gene, nucleotides 406-1155 of the *gag* gene, or nucleotides 1-2673 of the *env* gene of HIV-2. Other embodiments of the invention specifically define the HIV-2 probe sequences, either by the nucleotide sequence or the amino acid sequence it encodes. Six such sequences are provided.

The invention is further directed to a method of producing the HIV-2 specific hybridization probe by preparing a nucleic acid insert, introducing it into a recombinant cloning vector, transforming a cellular host, and recovering DNA recombinants.

The probe can comprise recombinant nucleic acid, and it can be optionally labeled.

VI. Issues

The only issue on appeal is whether the Examiner improperly rejected claims 90-109 under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description.

VII. Grouping of Claims

The claims, as rejected, do not stand or fall together. Appellants believe that certain dependent claims are separately patentable as they contain additional limitations. Specifically, claims 93-98 and 102-107 contain specific DNA or amino acid sequences for the HIV-2 probes. These sequences were recited in original claims of the application, providing pending claims 93-98 and 102-107 with written description support.

VIII. Argument

A. The Law of Written Description

The test for sufficiency of support in an application is whether the disclosure reasonably conveys to the artisan that the inventor had possession of the claimed subject matter at the time of filing. *Ralston Purina Co. v. Far-Mar-Co.*, 772 F.2d 1570,

1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985). The law does not require more than that the application describes the invention with sufficient detail that a skilled artisan would conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997).

In making this determination, the specification as a whole must be considered. *In re Wright*, 866 F.2d 422, 424, 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989). This means that the written description requirement can be fulfilled by using various techniques including "words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 U.S.P.Q.2d at 1966.

B. Rejection of Claims 90-109 Under 35 U.S.C. § 112, First Paragraph

1. The Examiner's Position

Claims 90-109 have been rejected under 35 U.S.C. § 112, first paragraph, as lacking written description support in the specification. The Office contends that the specification only provides a limited number of subgenomic HIV-2 clones, and that the specification fails to provide sufficient guidance pertaining to the nucleotide sequence of the inserts within these clones, with the exception of the LTR, *gag*, and *pol* [sic, *env*] genes described on pages 56-61 and Figures 6 and 7.

The Office further contends that the specification fails to provide the hybridization parameters that should be employed, and that melting temperatures are only disclosed

with regard to HIV-1 probes. The Office concludes that the specification does not provide any guidance pertaining to the identification, isolation, preparation, and use of HIV-2 specific probes under the claimed hybridization conditions. The Office cites case law in support of the contention that an adequate description of DNA requires a nucleotide sequence. Applicants disagree with the position of the Office.

2. The Written Description Support for the Claimed Invention

At the time the application was filed, Applicants had possession of **methods** for producing HIV-2 probes and for detecting HIV-2 nucleic acids. Upon reading the specification as a whole, the skilled artisan would conclude that Applicants had possession of the claimed **methods**. The Examiner's rejections suggest that Applicants are prosecuting composition claims, instead, and do not apply to the claimed methods.

Applicants are not claiming subgenomic HIV-2 clones, but instead are claiming methods of detecting HIV-2 retrovirus nucleic acids. The Examiner's citations of *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993) and *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997) are inapposite. These cases explore the application of the written description requirement to compositions. *Id.* The courts have not established

that the requirements for claiming a DNA sequence are the same as for using a DNA sequence in a method. The Examiner cannot simply ignore this issue.

Despite the Examiner's assertions otherwise, this application adequately discloses the claimed method. The application provides sequences for HIV-2 probes that will function effectively in the method. It also provides information on appropriate hybridization conditions for use in detecting the HIV-2 in the biological sample.

HIV-2 Probes

The application provides specific examples of sequences that will work appropriately in the method. The written description requirement may be satisfied if the broader concept would naturally occur to one skilled in the art upon reading the earlier specification. *In re Smythe*, 480 F.2d 1376, 1384, 178 U.S.P.Q. 279, 285 (C.C.P.A. 1973).

The specification describes the total cDNA of HIV-2 and provides restriction maps of HIV-2. (Specification at Figs. 4-8). The specification describes subgenomic clones of HIV-2, which together reconstitute the complete HIV-2 ROD genome. (Specification at 26, lines 14-23.) The use of the lambda ROD 4 recombinant containing the total cDNA of HIV-2 as a probe under low stringency conditions is further described in Example II. (Specification at page 38, paragraph 2). Therefore, Applicants describe clones encompassing the entire genome of HIV-2. Consequently,

the skilled artisan would recognize that Applicants possessed HIV-2 probes that are capable of hybridizing to **any** region of the HIV-2 genome using the claimed methods.

In addition, sequences of *gag*, *env*, and LTR regions are described. (Specification at 68-88). Applicants also described using the 2 kilobase E2.1 HIV-2 insert as a probe. (Specification at 32-34). Thus, Applicants have provided nucleotide sequences of a representative number of HIV-2 specific probes, which will work in the claimed invention.

Furthermore, Applicants have recited a common structural feature of the members of the genus of probes, which will work in the claimed methodology, identifying which probes can be used in the claimed method. Specifically, Applicants have recited that the probes hybridize to HIV-2ROD genomic DNA under hybridization conditions of 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA, with washes in 2X SSC, 0.1% SDS at 25°C; 1X SSC, 0.1% SDS at 60°C; or 0.1X SSC, 0.1% SDS at 60°C. Applicants submit that this feature adequately describes the specific probes of the claimed invention.

Having read the specification, the skilled artisan would recognize that Applicants possessed many different HIV-2 probes that could be used in the claimed methods. The Office has provided no explanation of why the claimed **methods** are not described in the specification as required to support a rejection under 35 U.S.C. § 112, first paragraph. See *In re Wertheim*, 541 F.2d 257, 265, 191 U.S.P.Q. 90, 98 (C.C.P.A.

1976). Instead, the Office appears to require that Applicants provide a nucleotide sequence of all probes that can be used in the claimed **methods**. Applicants submit that the focus of the inquiry should not be not whether Applicants have described every probe that can be used in the claimed **methods**, but whether Applicants have described the claimed **methods**. Applicants need not describe all species that a claim encompasses to fulfill the written description requirement. *Utter v. Hiraga* 845 F.2d 993, 998, 6 U.S.P.Q.2d 1709, 1714 (Fed. Cir. 1988). Applicants do not claim the various sequences that can be used in the method.

Consequently, Applicants need not provide the nucleotide sequence of all HIV-2 probes that can be used in the claimed methods. The skilled artisan would recognize that Applicants invented the methods encompassing a large genus of probes that could be used in the claimed methods. The claimed methods are broadly applicable, and Applicants have provided the requisite written description of these methods. Having read the specification, the skilled artisan would recognize that Applicants possessed **methods** of producing and using HIV-2 probes that are capable of hybridizing to any region of HIV-2. Therefore, Applicants have satisfied the written description requirement of 35 U.S.C. § 112, first paragraph.

Hybridization Conditions

Additionally, the application adequately discloses the hybridization conditions for use in the claimed method. Example II describes hybridization conditions of 37°C for

16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA (T_m -42°C). (Specification at page 35, paragraph 2). The specification describes washing hybridizations with the lambda ROD 4 recombinant containing the total cDNA of HIV-2 successively in 2X SSC, 0.1% SDS at 25° (T_m -42°C); 1X SSC, 0.1% SDS at 60° (T_m -20°C); and 0.1X SSC, 0.1% SDS at 60° (T_m -3°C). (Specification at page 38, paragraph 2). Thus, contrary to the Office's assertion, the recited hybridization and wash conditions are disclosed with regard to hybridization with HIV-2 probes.

Furthermore, the specification describes dot-blot hybridization of a 2 kilobase HIV-2 probe to HIV-2 nucleic acid under stringent conditions. (Specification at page 40, paragraph 1, and pages 42-43, bridging paragraph). 11 of 11 isolates were identified as HIV-2 using this method. *Id.* The specification further describes that the invention relates to a DNA or RNA capable of hybridizing with HIV-2 DNA or RNA under non-stringent conditions. (Specification at 50, paragraph 1). The specification also describes that preferred embodiments include detecting HIV-2 nucleic acids under stringent and non-stringent conditions. (Specification at page 54, line 2, through page 55, line 4). Consequently, the skilled artisan would recognize that hybridization and wash conditions **recited in the specification** (i.e. hybridization at 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon

sperm DNA, with washes in 2X SSC, 0.1% SDS at 25°; 1X SSC, 0.1% SDS at 60°; or 0.1X SSC, 0.1% SDS at 60°) would be within the scope of the invention.

Having read the specification, the skilled artisan would recognize that Applicants possessed methods of producing and using HIV-2 probes that are capable of hybridizing to any region of HIV-2, under the hybridization conditions set forth. Therefore, Applicants have satisfied the written description requirement of 35 U.S.C. § 112, first paragraph.

3. Additional Arguments for Written Description

Claims 93-98 and 102-107 contain specific DNA or amino acid sequences for the HIV-2 probe. The sequences provided in these claims are supported in the application as originally filed. Claims 92-93 and 101-102 are supported in original dependent claims 37 and 41, which recite methods of producing and using HIV-2 probes, and dependent claim 29, which recites LTR sequences.

Claims 92, 94-97, 101, and 103-106 recite amino acid sequences found in original claims 30-33. Original claims encompass a nucleic acid coding for at least part of several HIV-2 Gag amino acid sequences recited in the claims.

Claims 92, 98, 101, and 107 recite amino acid sequences encompassed by original claim 34, which recites a nucleic acid coding for at least part of an HIV-2 Env amino acid sequence.

Having read the original claims, one skilled in the art would understand that Applicants had invented methods of detecting HIV-2 in a biological sample using the claimed sequences as a probe. Thus, the Examiner's rejection of these claims for lack of written description is improper.

IX. CONCLUSION

In view of the foregoing remarks, Appellant respectfully submits that the rejection of claims 90-109 under 35 U.S.C. § 112, first paragraph, is in error and should be reversed.

Respectfully submitted,

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APPENDIX

90. A method of detecting HIV-2 retrovirus nucleic acid in a biological sample, said method comprising:

a) contacting said sample with an HIV-2 specific probe under hybridization conditions selected from the group consisting of hybridization conditions of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe, wherein said probe comprises an HIV-2 nucleic acid molecule, which hybridizes to HIV-2ROD genomic DNA under hybridization conditions selected from the group consisting of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe;

b) washing the resulting hybrid under conditions selected from the group consisting of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe; and

c) detecting said hybrid.

91. The method of claim 90, wherein said probe comprises cDNA.

92. A method of detecting HIV-2 retrovirus nucleic acid in a biological sample, said method comprising:

a) contacting said sample with an HIV-2 specific probe under hybridization conditions selected from the group consisting of hybridization conditions of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe,

wherein said probe comprises an HIV-2 nucleic acid molecule obtained from nucleotides 1-380 of the U3/R region of HIV-2, nucleotides 1-1566 of the *gag* gene of HIV-2, nucleotides 1114-1524 of the *gag* gene, nucleotides 1-405 of the *gag* gene, nucleotides 406-1155 of the *gag* gene, or nucleotides 1-2673 of the *env* gene of HIV-2, and

wherein said probe hybridizes to HIV-2ROD genomic DNA under hybridization conditions selected from the group consisting of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe;

b) washing the resulting hybrid under conditions selected from the group consisting of 42°C below the melting temperature of the probe, 20°C below the melting temperature of the probe, and 3°C below the melting temperature of the probe; and

c) detecting said hybrid.

93. The method of claim 92, wherein said probe is obtained from the following sequence:

GTGGAAGGCG	AGACTGAAAG	CAAGAGGAAT	ACCATTTAGT	TAAAGGACAG
GAACAGCTAT	ACTTGGTCAG	GGCAGGAAGT	AACTAACAGA	AACAGCTGAG
ACTGCAGGGA	CTTTCCAGAA	GGGGCTGTAA	CCAAGGGAGG	GACATGGGAG
GAGCTGGTGG	GGAACGCCTC	ATATTCTCTG	TATAATATAC	CCGCTGCTTG
CATTGTACTT	CAGTCGCTCT	GCGGAGAGGC	TGGCAGATTG	AGCCCTGGAG
GATCTCTCCA	GCACTAGACG	GATGAGCCTG	GGTGCCCTGC	TAGACTCTCA
CCAGCACTTG	GCCGGTGCTG	GCAGACGGCC	CCACGCTTGC	CTGCTTAAAA
ACCTTCCTTA	ATAAAGCTGC	AGTAGAAGCA.		

94. The method of claim 92, wherein said probe encodes the following amino acid sequence:

Met	Gly	Ala	Arg	Asn	Ser	Val	Leu	Arg	Gly	Lys	Lys	Ala	Asp	Glu	Leu
Glu	Arg	Ile	Arg	Leu	Arg	Pro	Gly	Gly	Lys	Lys	Lys	Tyr	Arg	Leu	Lys
His	Ile	Val	Trp	Ala	Ala	Asn	Lys	Leu	Asp	Arg	Phe	Gly	Leu	Ala	Glu
Ser	Leu	Leu	Glu	Ser	Lys	Glu	Gly	Cys	Gln	Lys	Ile	Leu	Thr	Val	Leu
Asp	Pro	Met	Val	Pro	Thr	Gly	Ser	Glu	Asn	Leu	Lys	Ser	Leu	Phe	Asn
Thr	Val	Cys	Val	Ile	Trp	Cys	Ile	His	Ala	Glu	Glu	Lys	Val	Lys	Asp
Thr	Glu	Gly	Ala	Lys	Gln	Ile	Val	Arg	Arg	His	Leu	Val	Ala	Glu	Thr
Gly	Thr	Ala	Glu	Lys	Met	Pro	Ser	Thr	Ser	Arg	Pro	Thr	Ala	Pro	Ser
Ser	Glu	Lys	Gly	Gly	Asn	Tyr	Pro	Val	Gln	His	Val	Gly	Gly	Asn	Tyr
Thr	His	Ile	Pro	Leu	Ser	Pro	Arg	Thr	Leu	Asn	Ala	Trp	Val	Lys	Leu
Val	Glu	Glu	Lys	Lys	Phe	Gly	Ala	Glu	Val	Val	Pro	Gly	Phe	Gln	Ala
Leu	Ser	Glu	Gly	Cys	Thr	Pro	Tyr	Asp	Ile	Asn	Gln	Met	Leu	Asn	Cys
Val	Gly	Asp	His	Gln	Ala	Ala	Met	Gln	Ile	Ile	Arg	Glu	Ile	Ile	Asn
Glu	Glu	Ala	Ala	Glu	Trp	Asp	Val	Gln	His	Pro	Ile	Pro	Gly	Pro	Leu
Pro	Ala	Gly	Gln	Leu	Arg	Glu	Pro	Arg	Gly	Ser	Asp	Ile	Ala	Gly	Thr
Thr	Ser	Thr	Val	Glu	Glu	Gln	Ile	Gln	Trp	Met	Phe	Arg	Pro	Gln	Asn
Pro	Val	Pro	Val	Gly	Asn	Ile	Tyr	Arg	Arg	Trp	Ile	Gln	Ile	Gly	Leu
Gln	Lys	Cys	Val	Arg	Met	Tyr	Asn	Pro	Thr	Asn	Ile	Leu	Asp	Ile	Lys
Gln	Gly	Pro	Lys	Glu	Pro	Phe	Gln	Ser	Tyr	Val	Asp	Arg	Phe	Tyr	Lys
Ser	Leu	Arg	Ala	Glu	Gln	Thr	Asp	Pro	Ala	Val	Lys	Asn	Trp	Met	Thr
Gln	Thr	Leu	Leu	Val	Gln	Asn	Ala	Asn	Pro	Asp	Cys	Lys	Leu	Val	Leu
Lys	Gly	Leu	Gly	Met	Asn	Pro	Thr	Leu	Glu	Glu	Met	Leu	Thr	Ala	Cys
Gln	Gly	Val	Gly	Gly	Pro	Gly	Gln	Lys	Ala	Arg	Leu	Met	Ala	Glu	Ala

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Leu Lys Glu Val Ile Gly Pro Ala Pro Ile Pro Phe Ala Ala Ala Gln
Gln Arg Lys Ala Phe Lys Cys Trp Asn Cys Gly Lys Glu Gly His Ser
Ala Arg Gln Cys Arg Ala Pro Arg Arg Gln Gly Cys Trp Lys Cys Gly
Lys Pro Gly His Ile Met Thr Asn Cys Pro Asp Arg Gln Ala Gly Phe
Leu Gly Leu Gly Pro Trp Gly Lys Lys Pro Arg Asn Phe Pro Val Ala
Gln Val Pro Gln Gly Leu Thr Pro Thr Ala Pro Pro Val Asp Pro Ala
Val Asp Leu Leu Glu Lys Tyr Met Gln Gln Gly Lys Arg Gln Arg Glu
Gln Arg Glu Arg Pro Tyr Lys Glu Val Thr Glu Asp Leu Leu His Leu
Glu Gln Gly Glu Thr Pro Tyr Arg Glu Pro Pro Thr Glu Asp Leu Leu
His Leu Asn Ser Leu Phe Gly Lys Asp Gln.

95. The method of claim 92, wherein said probe encodes the following amino acid sequence:

Arg Lys Ala Phe Lys Cys Trp Asn Cys Gly Lys Glu Gly His Ser Ala
Arg Gln Cys Arg Ala Pro Arg Arg Gln Gly Cys Trp Lys Cys Gly Lys
Pro Gly His Ile Met Thr Asn Cys Pro Asp Arg Gln Ala Gly Phe Leu
Gly Leu Gly Pro Trp Gly Lys Lys Pro Arg Asn Phe Pro Val Ala Gln
Val Pro Gln Gly Leu Thr Pro Thr Ala Pro Pro Val Asp Pro Ala Val
Asp Leu Leu Glu Lys Tyr Met Gln Gln Gly Lys Arg Gln Arg Glu Gln
Arg Glu Arg Pro Tyr Lys Glu Val Thr Glu Asp Leu Leu His Leu Glu
Gln Gly Glu Thr Pro Tyr Arg Glu Pro Pro Thr Glu Asp Leu Leu His
Leu Asn Ser Leu Phe Gly Lys Asp Gln.

96. The method of claim 92, wherein said probe encodes the following amino acid sequence:

Met Gly Ala Arg Asn Ser Val Leu Arg Gly Lys Lys Ala Asp Glu Leu
Glu Arg Ile Arg Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Leu Lys
His Ile Val Trp Ala Ala Asn Lys Leu Asp Arg Phe Gly Leu Ala Glu
Ser Leu Leu Glu Ser Lys Glu Gly Cys Gln Lys Ile Leu Thr Val Leu
Asp Pro Met Val Pro Thr Gly Ser Glu Asn Leu Lys Ser Leu Phe Asn
Thr Val Cys Val Ile Trp Cys Ile His Ala Glu Glu Lys Val Lys Asp
Thr Glu Gly Ala Lys Gln Ile Val Arg Arg His Leu Val Ala Glu Thr
Gly Thr Ala Glu Lys Met Pro Ser Thr Ser Arg Pro Thr Ala Pro Ser
Ser Glu Lys Gly Gly Asn Tyr.

97. The method of claim 92, wherein said probe encodes the following amino acid sequence:

Pro Val Gln His Val Gly Gly Asn Tyr Thr His Ile Pro Leu Ser Pro
Arg Thr Leu Asn Ala Trp Val Lys Leu Val Glu Glu Lys Lys Phe Gly
Ala Glu Val Val Pro Gly Phe Gln Ala Leu Ser Glu Gly Cys Thr Pro
Tyr Asp Ile Asn Gln Met Leu Asn Cys Val Gly Asp His Gln Ala Ala

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Met Gln Ile Ile Arg Glu Ile Ile Asn Glu Glu Ala Ala Glu Trp Asp
Val Gln His Pro Ile Pro Gly Pro Leu Pro Ala Gly Gln Leu Arg Glu
Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Val Glu Glu Gln
Ile Gln Trp Met Phe Arg Pro Gln Asn Pro Val Pro Val Gly Asn Ile
Tyr Arg Arg Trp Ile Gln Ile Gly Leu Gln Lys Cys Val Arg Met Tyr
Asn Pro Thr Asn Ile Leu Asp Ile Lys Gln Gly Pro Lys Glu Pro Phe
Gln Ser Tyr Val Asp Arg Phe Tyr Lys Ser Leu Arg Ala Glu Gln Thr
Asp Pro Ala Val Lys Asn Trp Met Thr Gln Thr Leu Leu Val Gln Asn
Ala Asn Pro Asp Cys Lys Leu Val Leu Lys Gly Leu Gly Met Asn Pro
Thr Leu Glu Glu Met Leu Thr Ala Cys Gln Gly Val Gly Gly Pro Gly
Gln Lys Ala Arg Leu Met Ala Glu Ala Leu Lys Glu Val Ile Gly Pro
Ala Pro Ile Pro Phe Ala Ala Ala Gln Gln.

98. The method of claim 92, wherein said probe encodes the following amino acid sequence:

Met Met Asn Gln Leu Leu Ile Ala Ile Leu Leu Ala Ser Ala Cys Leu
Val Tyr Cys Thr Gln Tyr Val Thr Val Phe Tyr Gly Val Pro Thr Trp
Lys Asn Ala Thr Ile Pro Leu Phe Cys Ala Thr Arg Asn Arg Asp Thr
Trp Gly Thr Ile Gln Cys Leu Pro Asp Asn Asp Asp Tyr Gln Glu Ile
Thr Leu Asn Val Thr Glu Ala Phe Asp Ala Trp Asn Asn Thr Val Thr
Glu Gln Ala Ile Glu Asp Val Trp His Leu Phe Glu Thr Ser Ile Lys
Pro Cys Val Lys Leu Thr Pro Leu Cys Val Ala Met Lys Cys Ser Ser
Thr Glu Ser Ser Thr Gly Asn Asn Thr Thr Ser Lys Ser Thr Ser Thr
Thr Thr Thr Thr Pro Thr Asp Gln Glu Gln Glu Ile Ser Glu Asp Thr
Pro Cys Ala Arg Ala Asp Asn Cys Ser Gly Leu Gly Glu Glu Glu Thr
Ile Asn Cys Gln Phe Asn Met Thr Gly leu Glu Arg Asp Lys Lys Lys
Gln Tyr Asn Glu Thr Trp Tyr Ser Lys Asp Val Val Cys Glu Thr Asn
Asn Ser Thr Asn Gln Thr Gln Cys Tyr Met Asn His Cys Asn Thr Ser
Val Ile Thr Glu Ser Cys Asp Lys His Tyr Trp Asp Ala Ile Arg Phe
Arg Tyr Cys Ala Pro Pro Gly Tyr Ala Leu Leu Arg Cys Asn Asp Thr
Asn Tyr Ser Gly Phe Ala Pro Asn Cys Ser Lys Val Val Ala Ser Thr
Cys Thr Arg Met Met Glu Thr Gln Thr Ser Thr Trp Phe Gly Phe Asn
Gly Thr Arg Ala Glu Asn Arg Thr Tyr Ile Tyr Trp His Gly Arg Asp
Asn Arg Thr Ile Ile Ser Leu Asn Lys Tyr Tyr Asn Leu Ser Leu His
Cys Lys Arg Pro Gly Asn Lys Thr Val Lys Gln Ile Met Leu Met Ser
Gly His Val Phe His Ser His Tyr Gln Pro Ile Asn Lys Arg Pro Arg
Gln Ala Trp Cys Trp Phe Lys Gly Lys Trp Lys Asp Ala Met Gln Glu
Val Lys Thr Leu Ala Lys His Pro Arg Tyr Arg Gly Thr Asn Asp Thr
Arg Asn Ile Ser Phe Ala Ala Pro Gly Lys Gly Ser Asp Pro Glu Val
Ala Tyr Met Trp Thr Asn Cys Arg Gly Glu Phe Leu Tyr Cys Asn Met
Thr Trp Phe Leu Asn Trp Ile Glu Asn Lys Thr His Arg Asn Tyr Ala
Pro Cys His Ile Lys Gln Ile Ile Asn Thr Trp His Lys Val Gly Arg
Asn Val Tyr Leu Pro Pro Arg Glu Gly Glu Leu Ser Cys Asn Ser Thr
Val Thr Ser Ile Ile Ala Asn Ile Asp Trp Gln Asn Asn Asn Gln Thr

Asn Ile Thr Phe Ser Ala Glu Val Ala Glu Leu Tyr Arg Leu Glu Leu
Gly Asp Tyr Lys Leu Val Glu Ile Thr Pro Ile Gly Phe Ala Pro Thr
Lys Glu Lys Arg Tyr Ser Ser Ala His Gly Arg His Thr Arg Gly Val
Phe Val Leu Gly Phe Leu Gly Phe Leu Ala Thr Ala Gly Ser Ala Met
Gly Ala Arg Ala Ser Leu Thr Val Ser Ala Gln Ser Arg Thr Leu Leu
Ala Gly Ile Val Gln Gln Gln Gln Gln Leu Leu Asp Val Val Lys Arg
Gln Gln Glu Leu Leu Arg Leu Thr Val Trp Gly Thr Lys Asn Leu Gln
Ala Arg Val Thr Ala Ile Glu Lys Tyr Leu Gln Asp Gln Ala Arg Leu
Asn Ser Trp Gly Cys Ala Phe Arg Gln Val Cys His Thr Thr Val Pro
Trp Val Asn Asp Ser Leu Ala Pro Asp Trp Asp Asn Met Thr Trp Gln
Glu Trp Glu Lys Gln Val Arg Tyr Leu Glu Ala Asn Ile Ser Lys Ser
Leu Glu Gln Ala Gln Ile Gln Gln Glu Lys Asn Met Tyr Glu Leu Gln
Lys Leu Asn Ser Trp Asp Ile Phe Gly Asn Trp Phe Asp Leu Thr Ser
Trp Val Lys Tyr Ile Gln Tyr Gly Val Leu Ile Ile Val Ala Val Ile
Ala Leu Arg Ile Val Ile Tyr Val Val Gln Met Leu Ser Arg Leu Arg
Lys Gly Tyr Arg Pro Val Phe Ser Ser Pro Pro Gly Tyr Ile Gln Gln
Ile His Ile His Lys Asp Arg Gly Gln Pro Ala Asn Glu Glu Thr Glu
Glu Asp Gly Gly Ser Asn Gly Gly Asp Arg Tyr Trp Pro Trp Pro Ile
Ala Tyr Ile His Phe Leu Ile Arg Gln Leu Ile Arg Leu Leu Thr Arg
Leu Tyr Ser Ile Cys Arg Asp Leu Leu Ser Arg Ser Phe Leu Thr Leu
Gln Leu Ile Tyr Gln Asn Leu Arg Asp Trp Leu Arg Leu Arg Thr Ala
Phe Leu Gln Tyr Gly Cys Glu Trp Ile Gln Glu Ala Phe Gln Ala Ala
Ala Arg Ala Thr Arg Glu Thr Leu Ala Gly Ala Cys Arg Gly Leu Trp
Arg Val Leu Glu Arg Ile Gly Arg Gly Ile Leu Ala Val Pro Arg Arg
Ile Arg Gln Gly Ala Glu Ile Ala Leu Leu *** Gly Thr Ala Val Ser
Ala Gly Arg Leu Tyr Glu
Tyr Ser Met Glu Gly Pro Ser Ser Arg Lys Gly Glu Lys Phe Val
Gln Ala Thr Lys Tyr Gly,

wherein *** indicates a stop codon.

99. A method of producing an HIV-2 specific hybridization probe for HIV-2 retrovirus nucleic acid, said method comprising:

a) preparing a nucleic acid insert, which hybridizes to HIV-2ROD genomic DNA under hybridization conditions selected from the group consisting of 42°C below the melting temperature of the insert, 20°C below the melting temperature of the insert, and 3°C below the melting temperature of the insert;

b) introducing the insert into a recombinant cloning vector;

c) introducing said vector into a competent cellular host; and

d) recovering the DNA recombinants.

100. The method of claim 99, wherein said probe comprises cDNA.

101. A method of producing an HIV-2 specific hybridization probe for HIV-2 retrovirus nucleic acid, said method comprising:

a) preparing a nucleic acid insert, wherein said insert is obtained from nucleotides 1-380 of the U3/R region of HIV-2, nucleotides 1-1566 of the *gag* gene of HIV-2, nucleotides 1114-1524 of the *gag* gene, nucleotides 1-405 of the *gag* gene, nucleotides 406-1155 of the *gag* gene, or nucleotides 1-2673 of the *env* gene of HIV-2, and wherein said insert hybridizes to HIV-2ROD genomic DNA under hybridization conditions selected from the group consisting of 42°C below the melting temperature of the insert, 20°C below the melting temperature of the insert, and 3°C below the melting temperature of the insert;

b) introducing the insert into a recombinant cloning vector;

c) introducing said vector into a competent cellular host; and

d) recovering the DNA recombinants.

102. The method of claim 101, wherein said insert is obtained from the following sequence:

GTGGAAGGCG	AGACTGAAAG	CAAGAGGAAT	ACCATTTAGT	TAAAGGACAG
GAACAGCTAT	ACTTGGTCAG	GGCAGGAAGT	AACTAACAGA	AACAGCTGAG
ACTGCAGGGA	CTTTCAGAA	GGGGCTGTAA	CCAAGGGAGG	GACATGGGAG
GAGCTGGTGG	GGAACGCCTC	ATATTCTCTG	TATAATATAC	CCGCTGCTTG
CATTGTACTT	CAGTCGCTCT	GCGGAGAGGC	TGGCAGATTG	AGCCCTGGAG
GATCTCTCCA	GCACTAGACG	GATGAGCCTG	GGTGCCCTGC	TAGACTCTCA
CCAGCACTTG	GCCGGTGCTG	GCAGACGGCC	CCACGCTTGC	CTGCTTAAAA
ACCTTCCTTA	ATAAAGCTGC	AGTAGAAGCA.		

103. The method of claim 101, wherein said insert encodes the following amino acid sequence:

Met Gly Ala Arg Asn Ser Val Leu Arg Gly Lys Lys Ala Asp Glu Leu
Glu Arg Ile Arg Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Leu Lys
His Ile Val Trp Ala Ala Asn Lys Leu Asp Arg Phe Gly Leu Ala Glu
Ser Leu Leu Glu Ser Lys Glu Gly Cys Gln Lys Ile Leu Thr Val Leu
Asp Pro Met Val Pro Thr Gly Ser Glu Asn Leu Lys Ser Leu Phe Asn
Thr Val Cys Val Ile Trp Cys Ile His Ala Glu Glu Lys Val Lys Asp
Thr Glu Gly Ala Lys Gln Ile Val Arg Arg His Leu Val Ala Glu Thr
Gly Thr Ala Glu Lys Met Pro Ser Thr Ser Arg Pro Thr Ala Pro Ser
Ser Glu Lys Gly Gly Asn Tyr Pro Val Gln His Val Gly Gly Asn Tyr
Thr His Ile Pro Leu Ser Pro Arg Thr Leu Asn Ala Trp Val Lys Leu
Val Glu Glu Lys Lys Phe Gly Ala Glu Val Val Pro Gly Phe Gln Ala
Leu Ser Glu Gly Cys Thr Pro Tyr Asp Ile Asn Gln Met Leu Asn Cys
Val Gly Asp His Gln Ala Ala Met Gln Ile Ile Arg Glu Ile Ile Asn
Glu Glu Ala Ala Glu Trp Asp Val Gln His Pro Ile Pro Gly Pro Leu
Pro Ala Gly Gln Leu Arg Glu Pro Arg Gly Ser Asp Ile Ala Gly Thr
Thr Ser Thr Val Glu Glu Gln Ile Gln Trp Met Phe Arg Pro Gln Asn
Pro Val Pro Val Gly Asn Ile Tyr Arg Arg Trp Ile Gln Ile Gly Leu
Gln Lys Cys Val Arg Met Tyr Asn Pro Thr Asn Ile Leu Asp Ile Lys
Gln Gly Pro Lys Glu Pro Phe Gln Ser Tyr Val Asp Arg Phe Tyr Lys
Ser Leu Arg Ala Glu Gln Thr Asp Pro Ala Val Lys Asn Trp Met Thr
Gln Thr Leu Leu Val Gln Asn Ala Asn Pro Asp Cys Lys Leu Val Leu
Lys Gly Leu Gly Met Asn Pro Thr Leu Glu Glu Met Leu Thr Ala Cys
Gln Gly Val Gly Gly Pro Gly Gln Lys Ala Arg Leu Met Ala Glu Ala
Leu Lys Glu Val Ile Gly Pro Ala Pro Ile Pro Phe Ala Ala Ala Gln
Gln Arg Lys Ala Phe Lys Cys Trp Asn Cys Gly Lys Glu Gly His Ser
Ala Arg Gln Cys Arg Ala Pro Arg Arg Gln Gly Cys Trp Lys Cys Gly
Lys Pro Gly His Ile Met Thr Asn Cys Pro Asp Arg Gln Ala Gly Phe
Leu Gly Leu Gly Pro Trp Gly Lys Lys Pro Arg Asn Phe Pro Val Ala
Gln Val Pro Gln Gly Leu Thr Pro Thr Ala Pro Pro Val Asp Pro Ala
Val Asp Leu Leu Glu Lys Tyr Met Gln Gln Gly Lys Arg Gln Arg Glu
Gln Arg Glu Arg Pro Tyr Lys Glu Val Thr Glu Asp Leu Leu His Leu
Glu Gln Gly Glu Thr Pro Tyr Arg Glu Pro Pro Thr Glu Asp Leu Leu
His Leu Asn Ser Leu Phe Gly Lys Asp Gln.

104. The method of claim 101, wherein said insert encodes the following amino acid sequence:

Arg Lys Ala Phe Lys Cys Trp Asn Cys Gly Lys Glu Gly His Ser Ala
Arg Gln Cys Arg Ala Pro Arg Arg Gln Gly Cys Trp Lys Cys Gly Lys
Pro Gly His Ile Met Thr Asn Cys Pro Asp Arg Gln Ala Gly Phe Leu
Gly Leu Gly Pro Trp Gly Lys Lys Pro Arg Asn Phe Pro Val Ala Gln

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Val Pro Gln Gly Leu Thr Pro Thr Ala Pro Pro Val Asp Pro Ala Val
Asp Leu Leu Glu Lys Tyr Met Gln Gln Gly Lys Arg Gln Arg Glu Gln
Arg Glu Arg Pro Tyr Lys Glu Val Thr Glu Asp Leu Leu His Leu Glu
Gln Gly Glu Thr Pro Tyr Arg Glu Pro Pro Thr Glu Asp Leu Leu His
Leu Asn Ser Leu Phe Gly Lys Asp Gln.

105. The method of claim 101, wherein said insert encodes the following amino acid sequence:

Met Gly Ala Arg Asn Ser Val Leu Arg Gly Lys Lys Ala Asp Glu Leu
Glu Arg Ile Arg Leu Arg Pro Gly Gly Lys Lys Lys Tyr Arg Leu Lys
His Ile Val Trp Ala Ala Asn Lys Leu Asp Arg Phe Gly Leu Ala Glu
Ser Leu Leu Glu Ser Lys Glu Gly Cys Gln Lys Ile Leu Thr Val Leu
Asp Pro Met Val Pro Thr Gly Ser Glu Asn Leu Lys Ser Leu Phe Asn
Thr Val Cys Val Ile Trp Cys Ile His Ala Glu Glu Lys Val Lys Asp
Thr Glu Gly Ala Lys Gln Ile Val Arg Arg His Leu Val Ala Glu Thr
Gly Thr Ala Glu Lys Met Pro Ser Thr Ser Arg Pro Thr Ala Pro Ser
Ser Glu Lys Gly Gly Asn Tyr.

106. The method of claim 101, wherein said insert encodes the following amino acid sequence:

Pro Val Gln His Val Gly Gly Asn Tyr Thr His Ile Pro Leu Ser Pro
Arg Thr Leu Asn Ala Trp Val Lys Leu Val Glu Glu Lys Lys Phe Gly
Ala Glu Val Val Pro Gly Phe Gln Ala Leu Ser Glu Gly Cys Thr Pro
Tyr Asp Ile Asn Gln Met Leu Asn Cys Val Gly Asp His Gln Ala Ala
Met Gln Ile Ile Arg Glu Ile Ile Asn Glu Glu Ala Ala Glu Trp Asp
Val Gln His Pro Ile Pro Gly Pro Leu Pro Ala Gly Gln Leu Arg Glu
Pro Arg Gly Ser Asp Ile Ala Gly Thr Thr Ser Thr Val Glu Glu Gln
Ile Gln Trp Met Phe Arg Pro Gln Asn Pro Val Pro Val Gly Asn Ile
Tyr Arg Arg Trp Ile Gln Ile Gly Leu Gln Lys Cys Val Arg Met Tyr
Asn Pro Thr Asn Ile Leu Asp Ile Lys Gln Gly Pro Lys Glu Pro Phe
Gln Ser Tyr Val Asp Arg Phe Tyr Lys Ser Leu Arg Ala Glu Gln Thr
Asp Pro Ala Val Lys Asn Trp Met Thr Gln Thr Leu Leu Val Gln Asn
Ala Asn Pro Asp Cys Lys Leu Val Leu Lys Gly Leu Gly Met Asn Pro
Thr Leu Glu Glu Met Leu Thr Ala Cys Gln Gly Val Gly Gly Pro Gly
Gln Lys Ala Arg Leu Met Ala Glu Ala Leu Lys Glu Val Ile Gly Pro
Ala Pro Ile Pro Phe Ala Ala Ala Gln Gln.

107. The method of claim 101, wherein said insert encodes the following amino acid sequence:

Met Met Asn Gln Leu Leu Ile Ala Ile Leu Leu Ala Ser Ala Cys Leu
Val Tyr Cys Thr Gln Tyr Val Thr Val Phe Tyr Gly Val Pro Thr Trp

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Lys Asn Ala Thr Ile Pro Leu Phe Cys Ala Thr Arg Asn Arg Asp Thr
Trp Gly Thr Ile Gln Cys Leu Pro Asp Asn Asp Asp Tyr Gln Glu Ile
Thr Leu Asn Val Thr Glu Ala Phe Asp Ala Trp Asn Asn Thr Val Thr
Glu Gln Ala Ile Glu Asp Val Trp His Leu Phe Glu Thr Ser Ile Lys
Pro Cys Val Lys Leu Thr Pro Leu Cys Val Ala Met Lys Cys Ser Ser
Thr Glu Ser Ser Thr Gly Asn Asn Thr Thr Ser Lys Ser Thr Ser Thr
Thr Thr Thr Thr Pro Thr Asp Gln Glu Gln Glu Ile Ser Glu Asp Thr
Pro Cys Ala Arg Ala Asp Asn Cys Ser Gly Leu Gly Glu Glu Glu Thr
Ile Asn Cys Gln Phe Asn Met Thr Gly leu Glu Arg Asp Lys Lys Lys
Gln Tyr Asn Glu Thr Trp Tyr Ser Lys Asp Val Val Cys Glu Thr Asn
Asn Ser Thr Asn Gln Thr Gln Cys Tyr Met Asn His Cys Asn Thr Ser
Val Ile Thr Glu Ser Cys Asp Lys His Tyr Trp Asp Ala Ile Arg Phe
Arg Tyr Cys Ala Pro Pro Gly Tyr Ala Leu Leu Arg Cys Asn Asp Thr
Asn Tyr Ser Gly Phe Ala Pro Asn Cys Ser Lys Val Val Ala Ser Thr
Cys Thr Arg Met Met Glu Thr Gln Thr Ser Thr Trp Phe Gly Phe Asn
Gly Thr Arg Ala Glu Asn Arg Thr Tyr Ile Tyr Trp His Gly Arg Asp
Asn Arg Thr Ile Ile Ser Leu Asn Lys Tyr Tyr Asn Leu Ser Leu His
Cys Lys Arg Pro Gly Asn Lys Thr Val Lys Gln Ile Met Leu Met Ser
Gly His Val Phe His Ser His Tyr Gln Pro Ile Asn Lys Arg Pro Arg
Gln Ala Trp Cys Trp Phe Lys Gly Lys Trp Lys Asp Ala Met Gln Glu
Val Lys Thr Leu Ala Lys His Pro Arg Tyr Arg Gly Thr Asn Asp Thr
Arg Asn Ile Ser Phe Ala Ala Pro Gly Lys Gly Ser Asp Pro Glu Val
Ala Tyr Met Trp Thr Asn Cys Arg Gly Glu Phe Leu Tyr Cys Asn Met
Thr Trp Phe Leu Asn Trp Ile Glu Asn Lys Thr His Arg Asn Tyr Ala
Pro Cys His Ile Lys Gln Ile Ile Asn Thr Trp His Lys Val Gly Arg
Asn Val Tyr Leu Pro Pro Arg Glu Gly Glu Leu Ser Cys Asn Ser Thr
Val Thr Ser Ile Ile Ala Asn Ile Asp Trp Gln Asn Asn Asn Gln Thr
Asn Ile Thr Phe Ser Ala Glu Val Ala Glu Leu Tyr Arg Leu Glu Leu
Gly Asp Tyr Lys Leu Val Glu Ile Thr Pro Ile Gly Phe Ala Pro Thr
Lys Glu Lys Arg Tyr Ser Ser Ala His Gly Arg His Thr Arg Gly Val
Phe Val Leu Gly Phe Leu Gly Phe Leu Ala Thr Ala Gly Ser Ala Met
Gly Ala Arg Ala Ser Leu Thr Val Ser Ala Gln Ser Arg Thr Leu Leu
Ala Gly Ile Val Gln Gln Gln Gln Gln Leu Leu Asp Val Val Lys Arg
Gln Gln Glu Leu Leu Arg Leu Thr Val Trp Gly Thr Lys Asn Leu Gln
Ala Arg Val Thr Ala Ile Glu Lys Tyr Leu Gln Asp Gln Ala Arg Leu
Asn Ser Trp Gly Cys Ala Phe Arg Gln Val Cys His Thr Thr Val Pro
Trp Val Asn Asp Ser Leu Ala Pro Asp Trp Asp Asn Met Thr Trp Gln
Glu Trp Glu Lys Gln Val Arg Tyr Leu Glu Ala Asn Ile Ser Lys Ser
Leu Glu Gln Ala Gln Ile Gln Gln Glu Lys Asn Met Tyr Glu Leu Gln
Lys Leu Asn Ser Trp Asp Ile Phe Gly Asn Trp Phe Asp Leu Thr Ser
Trp Val Lys Tyr Ile Gln Tyr Gly Val Leu Ile Ile Val Ala Val Ile
Ala Leu Arg Ile Val Ile Tyr Val Val Gln Met Leu Ser Arg Leu Arg
Lys Gly Tyr Arg Pro Val Phe Ser Ser Pro Pro Gly Tyr Ile Gln Gln
Ile His Ile His Lys Asp Arg Gly Gln Pro Ala Asn Glu Glu Thr Glu
Glu Asp Gly Gly Ser Asn Gly Gly Asp Arg Tyr Trp Pro Trp Pro Ile

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Ala Tyr Ile His Phe Leu Ile Arg Gln Leu Ile Arg Leu Leu Thr Arg
Leu Tyr Ser Ile Cys Arg Asp Leu Leu Ser Arg Ser Phe Leu Thr Leu
Gln Leu Ile Tyr Gln Asn Leu Arg Asp Trp Leu Arg Leu Arg Thr Ala
Phe Leu Gln Tyr Gly Cys Glu Trp Ile Gln Glu Ala Phe Gln Ala Ala
Ala Arg Ala Thr Arg Glu Thr Leu Ala Gly Ala Cys Arg Gly Leu Trp
Arg Val Leu Glu Arg Ile Gly Arg Gly Ile Leu Ala Val Pro Arg Arg
Ile Arg Gln Gly Ala Glu Ile Ala Leu Leu *** Gly Thr Ala Val Ser
Ala Gly Arg Leu Tyr Glu
Tyr Ser Met Glu Gly Pro Ser Ser Arg Lys Gly Glu Lys Phe Val
Gln Ala Thr Lys Tyr Gly,

wherein *** indicates a stop codon.

108. The method of any one of claims 90-107, wherein said probe comprises recombinant nucleic acid.

109. The method of claim 108, wherein said recombinant nucleic acid is labeled.